REMARKS

Phone Interview

Applicants would like to thank Examiner Kim for the phone conferences held on March 8 and 13, 2006, to discuss the rejection under 35 U.S. C. §112, first paragraph (new matter). During the phone conference on March 13, 2006, Examiner Kim stated that she will most likely withdraw the rejection when Applicants submit their arguments in writing, since there is support for "wherein the formulation does not include a liposome."

Status of Claims

Claims 2-7, 11, 13, 14, 16, 19, 31, 38, and 46-64 are currently pending and under examination. Claims 1, 8-10, 12, 15, 17, 18, 20-30, 32-37, and 39-45 have been canceled without prejudice or disclaimer of the subject matter claimed therein. New claims 61-64 have been added.

Amendments to the Claims

New claims 61-64 have been added. Representative support for the addition of claims 61 and 62 can be found in claims 48, 49, 54, and 55. Representative support for the addition of claims 63 and 64 can be found in original claim 34. The new claims do not include prohibited new matter.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

A. Claims 2-7, 11, 13-14, 16, 19, 31, 38 and 46-60 have been rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement.

The Office Action alleges that the specification while being enabling for a method of inducing an immune response by applying a formulation onto pretreated skin, does not reasonably provide enablement for a method of inducing an immune response by applying a formulation onto skin that is dry or intact. The Office Action also cites the factors set forth in *In re Wands* in support of their position.

Claims 2 and 38 and their dependent claims are directed to a method of inducing an immune response comprising applying a dry formulation to skin of a subject, wherein the formulation comprises at least one antigen and at least one adjuvant, and wherein the formulation does not include a liposome. New claims 61-64 are ultimately dependent upon claim 2 or 38,

and therefore include the features of claims 2 and 38. Applicants respectfully point out that the claims do not require that the level of immune response induced by the dry formulation be the same or higher than the immune response induced with pretreatment of the skin.

In the response submitted on October 7, 2005, Applicants selected representative examples from the specification as evidence showing induction of antibodies upon application of dry formulation to skin without pretreatment for showing enablement of the scope of the claims by the specification. Applicants reiterate the representative examples in this response.

As pointed out in the last response, the specification demonstrates in Example 1 that a dry powder formulation of Cholera toxin (CT) induced high levels of antibodies in mice when applied to skin (see, *e.g.*, page 38, lines 3 to 8). The data in Table 1 confirm that mice immunized on the skin with CT in the form of dry powder achieved high titers of antibody without pretreatment. Mice numbers 996, 997, 998, 999 were immunized on the skin with CT in the form of dry powder without pretreatment, and anti-CT antibodies in these mice were detected by ELISA two weeks after initial immunization. As shown in Table 1, the geometric mean of the 14-day titer for these mice is 4957 (ELISA Units), while their prebleed is < 5. Applicants respectfully point out that as indicated on page 38, lines 1 and 2 of the specification, the geometric mean is calculated from the subtracted titers (14-day titer minus prebleed).

Additionally, the data in Tables 2 and 3 summarize similar results for Examples 2 and 3, respectively, using immunizations with reduced amounts of CT (50 μg and 25 μg respectively) in powder form applied to the skin. In Table 2, mice numbers 11712 to 11716 and in Table 3, mice numbers 836 to 840 were immunized in a similar manner as in Table 1. Likewise, as shown in both of these tables, the mice developed antibodies against CT when CT was applied in dry form to the skin of the mice without pretreatment.

In addition, Examples 4 through 7 disclose data showing that dry formulations of different antigens induce an immune response when placed on the skin. In each Example, a specified amount of an antigen solubilized in a liquid solution was allowed to dry overnight to achieve a dry formulation. Then the dry formulation was placed on the skin of mice to test for an induction of an immune response. The data collected show an immune response to each antigen when a dry formulation of each antigen was placed on the skin of mice (Tables 4-11). The amount of antibodies induced by the dry formulation in each case is higher than that in the prebleed.

Although the amount of antibodies induced in Tables 1-11 may not be as high as the amount of antibodies induced after pretreatment of the skin, the dry formulation applied without pretreatment induced an immune response in these mice, since the 14-day titer had a higher level of anti-CT antibodies than the prebleed. As pointed out above, the claims do not require that the level of antibodies induced by the dry formulation applied to the skin be the same as or greater than that induced with pretreatment. The claims only require an induction of an immune response by the dry formulation. The data in Tables 1-11 show that applying a dry formulation to the skin without pretreatment induces an immune response.

Further, the attached §1.132 declaration by Dr. Diane Epperson also shows that a dry formulation containing antigen and adjuvant applied to the skin of a subject without pretreating the skin induces an immune response. Briefly, a dry formulation comprising influenza split virus and hemagglutinin applied to the skin of guinea pig induced an increase in antibody titers against the influenza strain (see graphs in declaration). The skin of the guinea pig was not hydrated or pretreated in any manner prior to application of the dry formulation.

In summary, these data clearly demonstrate that a dry powder formulation applied directly to the skin without pretreatment induces an immune response. The Examples describe in detail how the immunizations were accomplished thus teaching one skilled in the art how to use the claimed invention. Therefore, the specification provides sufficient guidance to enable one of ordinary skill in the art to make and use a dry formulation of antigens for inducing an immune response without undue experimentation. Applicants respectfully point out that the Examples in the specification describe in detail how the dry formulations are made, how they are applied, and how to test for induction of an immune response. Accordingly, the specification satisfies the requirements of enablement set forth by the Wands factors. Applicants respectfully request that this rejection be withdrawn.

B. Claims 2-7, 11, 13-14, 16, 19, 31, 38, and 46-60 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not provide written description for the claimed invention.

The Office Action alleges that the specification does not provide a written description for "wherein the formulation does not include a liposome." As set forth in the response submitted on October 7, 2005, original claim 37 provides support for the phrase. Since the claims as

originally filed are considered a part of the disclosure (MPEP 2163.06(III)), the phrase is supported by the disclosure as originally filed.

Furthermore, the specification as originally filed does not require that the antigen formulations contain liposomes. As an example, on page 18, lines 12 to 31 and page 25, lines 24 (onward) describe formulations prepared by mixing antigen with carriers or excipients that are not liposomes. Liposomes are only one of the many carriers that may be combined with an antigen to produce a formulation. Thus, the phrase "wherein the formulation contains liposomes" should not be considered to constitute new matter.

Previous Rejections under 35 U.S.C. § 102 and § 103

A. In the previous Office Action (dated July 8, 2005), claims 2-5, 7, 11, 13, 14, 16, 19, 31, 38, 46-48, 51-54, 56, and 58-60 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 5,910,306 and claims 2-7, 11, 13, 14, 16, 19, 31, 38, and 46-60 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 5,980,898.

The previous Office Action alleges that since the cited patents teach that liposome containing antigen and adjuvant can be lyophilized and discloses application of said formulation to dry skin of subject. Without acquiescing to the propriety of these rejections, Applicants inserted the phrase "wherein the formulation does not include a liposome" in the response (dated October 7, 2005) to the previous Office Action.

However, Applicants respectfully point out that the cited patents do not teach applying dry formulations comprising liposomes to the skin. Rather, the cited patents disclose that the formulations are prepared by mixing lyophilized liposomes with antigen that is dissolved or suspended in solution. Accordingly, the formulations comprising liposomes and antigen are wet solutions and not dry formulations (see U.S. Patent 5,910,306, col. 4, lines 33-35 and col. 12, Example 2; and U.S. Patent 5,980,898 col. 11, line 63 to 65 and col. 12, lines 36-39). The cited U.S. patents do not teach applying dry formulations comprising liposomes to the skin of a subject to induce an immune response.

B. In the previous Office Action, Claims 2, 6, 49, 55 and 57 were rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent 5,910,306 in view U.S. Patent 5,988,898.

Without acquiescing to the propriety of these rejections, Applicants inserted the phrase "wherein the formulation does not include a liposome" in the response (dated October 7, 2005) to the previous Office Action. The deficiencies of the cited patents are discussed immediately above. The cited references do not disclose applying dry formulations comprising an antigen to the skin of a subject to induce an immune response.

Rejections under 35 U.S.C. § 102

A. Claims 2-7, 11, 13, 14, 16, 19, 31, 38, 46-60 are rejected under 35 U.S.C. § 102 (e) as being anticipated by U.S. Patent 6,797,276.

As discussed above, claims 2 and 38 and their dependent claims are directed to a method of inducing an immune response comprising applying a dry formulation to skin of a subject, wherein the formulation comprises at least one antigen and at least one adjuvant, and wherein the formulation does not include a liposome. New claims 61-64 are ultimately dependent upon claim 2 or 38, and therefore include the features of claims 2 and 38.

The Office Action alleges that the cited patent teaches a method of inducing immune response comprising administering a dry formulation because the patent discloses that the antigenic formulation can be utilized with vehicles encompassing powder.

Applicants respectfully point out that the cited patent does not teach dry formulation. The cited patent discloses pretreatment of the skin prior to administering a formulation comprising an antigen. The paragraph (co. 8, line 25 of U.S. Patent 6,797,276) that the Office Action cited to only teaches that the skin may be hydrated or made permeable by using various vehicles including powder. The paragraph does not teach applying dry formulations comprising antigen to the skin of a subject. Rather, as shown in the Examples of U.S. Patent 6,797,276, the formulations that were applied to the skin of the subject were wet formulations, *i.e.* solutions. Thus, even if the cited patent teaches the use of a powder as a vehicle, the powder when combined with the antigen in solution would yield a wet formulation. Accordingly, the cited patent does not anticipate the claimed invention.

Non-Statutory Double Patenting

Claims 2-5, 11, 13, 14, 31, 38, 46-48, 50-54, 57, and 58 are rejected under the ground of

nonstatutory obviousness-type double patenting. Specifically, the claims have been rejected over claims 1-11 of U.S. Patent 6,797,276.

Respectfully, Applicants would like to point out that the claims of the present invention are directed to a method of inducing an immune response comprising applying a dry formulation to skin of a subject. Although the claims of U.S. Patent 6,797,276 are directed to a method of inducing an immune response, these claims do not comprise applying a formulation in dry form to the skin of a subject. As discussed above, U.S. Patent 6,797,276 does not disclose applying dry formulations to the skin of a subject for inducing an immune response. Therefore, Applicants assert that the claims in the instant application are patently distinct from the pending applications.

CONCLUSION

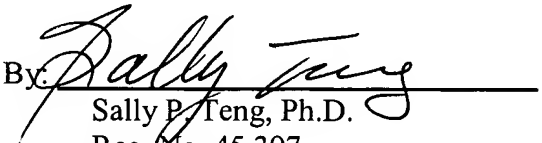
The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP

Dated: May 5, 2006

By: 
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